REMARKS

Favorable consideration of this application is respectfully requested in view of the above amendment and the following remarks.

Claims 1-14 and 16 are pending claim in this application. Claims 1-14 and 16 have been rejected. Claims 1 and 6 have been amended and claims 4 and 11 have been cancelled without prejudice. Applicants submit that no new matter has been added.

Claims 1-14 and 16 have been rejected under 35 U.S.C. §103(a) as being unpatentable over van der Burg, U.S. Patent Nos. 4,016,161 and 4,054,572 (the van der Burg patents). The Examiner states *inter alia*:

> ...applicants amendments and remarks have been fully considered but they are not found persuasive. The applicants stated that the Examiner has not identified a reason that would have led a chemist to select and modify a known compound in the van der Burg patents to arrive at the compound recited in claim 1 and that the van der Burg generic compound of formula I does not encompass the presently claimed compounds. However, the generic structure of van der Burg indicates that the –(CH2)nNR5R6 is attached to the piperidine ring in variable positions with the positions being labeled 1, 2, 3, and 4. It is noted that van der Burg specifically teaches compounds attached to the piperidine ring in the 2 and 3 position but as stated in the MPEP 2144.09 states "Compounds which are position isomers (compounds having the same radicals in physically different positions on the same nucleus)...are generally of sufficiently close structural similarity that there is a presumed expectation that such compound possess similar properties. In re Wilder, 563 F.2d 457, 195 USPQ 426 (CCPA 1977).
>
> The first point can be addressed by citing In re Deuel 34 USPQ2d 1210, 1214, which states, "Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties." This is clearly all the motivation necessary to render a species obvious. Thus as stated in the previous office action one of ordinary skill in the art would have been motivated to select 1-diethylamine from the generic teaching of van der Burg to prepare the compounds of the instant invention.

Applicants respectfully traverse this rejection and submit that the van der Burg patents do not establish a *prima facie* case of obviousness for the reasons set forth below.

With respect to obviousness of claimed compounds based on structural similarity to prior art compounds, the Examiner's attention is directed to the recently decided case, Proctor & Gamble Company v. Teva Pharmaceuticals, 566 F.3d 989, 995 (Fed. Cir. 2009). In particular, the Federal Circuit in Proctor & Gample instructed:

> An obviousness argument based on structural similarity between claimed and prior art compounds "clearly depends on a preliminary finding that one of ordinary skill in the art would have selected [the prior art compound] as a lead compound." Takeda, 492, F. 3d at 1359; see also Eisai Col. Lt. v. Dr. Reddy's Labs., Ltd., 533 F.3d 1353, 1359 (Fed. Cir. 2008) (stating that "post KSR, a prima facie case of obviousness for a chemical compound still, in general begins with the reasoned identification of a lead compound" in the prior art.

It is asserted that in the present case the Examiner has not identified a reason that would have led a chemist to select a compound in the van der Burg patents as a lead compound.

To this end, while the piperidine ring of the van der Burg compounds is labeled as positions 1, 2, 3 and 4, these compounds absolutely require that the –(CH2)n-NR5R6 moiety be attached only at positions 2 or 3 of the piperidine ring (see USP 4,054,572, column 1, lines 30-36 and USP 4,016,181, column 24, lines 37-44), whereas in the presently claimed compound the –(CH2)n-NR5R6 moiety is present only at position 1. Further, the requisite therapeutic activity of the compounds described in the van der Burgs patents is antidepressant activity (see e.g., U.S. Patent 4,054,572, column 9, lines 52-62), whereas the requisite therapeutic activity of the compounds of the presently claimed invention is progestagenic/anti-progestagenic activity. There is no teaching or any suggestion whatsoever that any of the van der Burg compounds having at position 2 or 3 a –(CH2)n-NR5R6 moiety would also possess progestagenic/anti-progestagenic activity.

In addition, in the previous Action dated June 13, 2008, the Examiner stated on page 4 that positional isomers of the compounds of the instant invention are at examples in column 15, liens 38-40, 44-47 and column 16, lines 8-10 and 40-41. However, there is no teaching or suggestion to

select from the greater than 80 described compounds a lead compound amongst the few 2-dimethylamino..oxazaepine compounds described in van der Burg for modification. No disclosure or evidence is presented in the van der Burg patents that the compounds pointed out by the Examiner were most therapeutically effective with respect to progestagenic/anti-progestagenic activity. Accordingly, the van der Burg patents would not have led a person of ordinary skill in the art to select one of the compounds mentioned by the Examiner as a lead compound for modification. Accordingly, the requirement by the Federal Circuit to have a reasoned identification of a lead compound to establish a *prima facie* case of obviousness has not been met by the Examiner.

Moreover, the Federal Circuit in Proctor & Gamble , 566 F.3d 989, 996 (Fed. Cir. 2009), also instructed that in situations where there is structural similarity between the claimed compound and the prior art compound there is a second requirement to establish a *prima facie* case of obviousness:

> As we noted in Takeda: A known compound may suggest its homolog, analog, or isomer because such compound often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties**….[However,] it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound** [emphasis in bolded type].

With respect to satisfying the second requirement that "it remain necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness of a new claimed compound", the van der Burg patents are directed to compounds having antidepressant activity. There is no indication whatsoever in the van der Burg patents that such compounds would possess progestagenic/anti-progestagenic activity. Indeed, the fact that the van der Burg patents disclose antidepressant activity and are completely silent with respect to progestagenic/anti-progestagenic activity begs the question as to why a person of ordinary skill in the art would consult the van der Burg patents for compounds possessing progestogenic/anti-progestagenic activity or to improve progestogenic/anti-progestagenic activity. Further, there is nothing in the van der Burg patents to suggest modifying the compounds by ring

walking, i.e., changing the required position of the –(CH2)n-NR5R6 moiety from 2 or 3 to 1 on the piperidine ring. Indeed, one skilled in the art faced with van der Burg's requirement that the –(CH2)n-NR5R6 moiety must be attached to the 2 or 3 position of the piperidine ring would be discouraged from modifying the piperidine ring to the 1 position to obtain improved antidepressant activity let alone progestogenic activity. In view of 1) the mere disclosure in the van der Burg patents that such compounds possess antidepressant activity and the lack of disclosure in these patents of progestagenic/anti-progestagenic activity, 2) the absolute requirement in the van der Burg patents that the –(CH2)n-NR5R6 moiety be attached to the 2 or 3 position of the piperidine ring, and 3) the lack of any guidance whatsoever in the van der Burg patents as to which specific modification would be successful in providing progestagenic/anti-progestagenic activity, one skilled in the art would not be motivated to modify the van der Burg compounds to possess a –(CH2)n-NR5R6 moiety at position 1 for the purpose of having progestagenic/anti-progestagenic activity. Thus, the claimed compounds are not rendered obvious by the van der Burg patents.

In view of the above, withdrawal of the rejection of claims 1-14 and 16 under 35 U.S.C. §103(a) is respectfully requested.

Claims 1-14 and 16 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 and 21 of copending application no. 11/861,427. The Examiner contends that while the conflicting claims are not identical, they are not patentably distinct from each other because the compound of the instant invention embraces the compounds of formula I of copending application no. 11/861,427 where R1 is H,; R2 is F; R3 is CN; R4 is H; R8 is H; R9 is H, R7 is H and R6 is C(O)-(1-4C) alkyl optionally substituted with one or more halogen atoms.

In response, Applicants request that this rejection be held in abeyance until indication by the Examiner that the pending claims are otherwise allowable.

Claims 1-14 and 16 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of copending application no. 12/115,983. The Examiner contends that while the conflicting claims are not identical, they are not patentably distinct from each other because the compound of the instant invention embraces the

compounds of formula I of copending application no. 12/115,983 where R1 is H; R4 is H; R8 is H; R9 is H, R7 is H and R6 is (1-5C)acyl, (1-5)thioacyl, (1-4C)alkylsulfonyl and (1-4C)alkoxycarbonyl, each optionally substituted with one or more halogen atoms.

In response, Applicants request that this rejection be held in abeyance until indication by the Examiner that the pending claims are otherwise allowable.

Claims 1-14 and 16 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. In particular, the Examiner contends that claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by R1-R5 and R9-R10 in the provisos labeled (i), (ii) and (iii) at the end of claim 1 which fails to set forth the metes and bounds of the range. The Examiner also contends that claims 4 and 11 are vague and indefinite in that it is not further limiting of claim 1. The Examiner also contends that claim 11 is vague and indefinite in that it is a duplicate of claim 4.

In response, to facilitate prosecution, claim 1 has been amended to further clarify the invention and claims 4 and 11 have been cancelled without prejudice.

In view of the above, withdrawal of the rejection of claims 1-14 and 16 under 35 U.S.C. §112, second paragraph, is respectfully requested.

A good faith effort has been made to place the present application in condition for allowance. If the Examiner believes a telephone conference would be of value, she is requested to call the undersigned at the number listed below.

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Respectfully submitted,

By 

Organon International Inc.
Patent Department
c/o Schering-Plough Corporation
2000 Galloping Hill Road
Kenilworth, New Jersey 07033-0530
K-6-1; MS 1990
Tel: (908) 298-2161
Fax: (908)-298-5388

Susan Hess
Registration No.: 37,350
Attorney For Applicant(s)

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